6-19-89

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

007252

JUN 19 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Glyphosate - EPA Registration Nos. 524-318 and 524-333 - Historical Control Data for Mouse Kidney Tumors

MRID No.: 00130406
Caswell No.: 661A
Record No.: 238,412
Project No.: 9-0697

FROM: William Dykstra, Reviewer
Review Section I
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

William Dykstra 6/9/89

TO: Robert J. Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (H7505C)

6/9/89

THRU: Edwin Budd, Acting Branch Chief
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

and

6/9/89

William Burnham, Deputy Director
Health Effects Division (H7509C)

Requested Action

Review historical control data on mouse kidney tumors submitted by Monsanto in response to meeting of November 10, 1988.

1 of 62

Conclusions and Recommendations

The historical control data showed that the incidence of renal neoplasms in male CD-1 mice ranged from 0 to 3.3 percent at Bio/dynamics (the laboratory that performed the glyphosate mouse oncogenicity study), 0 to 4.7 percent at Hazleton, 0 to 1.7 percent at IRDC, 0 to 3.3 percent at Litton Bionetics, and 0 to 1.4 percent in Japan (Japanese Institute for Environmental Toxicology). The range of incidences of 0 to 7.1 percent reported by Monsanto in their November 10, 1988 meeting with the Agency was taken from the data on F_1 male mice in reproduction studies at Hazleton.

These F_1 data could not be further substantiated by Monsanto and therefore, cannot be used to support the Monsanto position.

Other data study presented by Monsanto, briefly, were two chronic bioassays with male CD-1 mice in which the following incidences of renal neoplasms were noted:

	Control	Low	Mid	High
Study I	0/80	2/80	1/80	2/80
Study II	2/50	1/50	3/50	3/50

Monsanto cites these data as showing an incidence of 0 to 6 percent in control or treated groups (the occurrences of renal tumors in treated groups were not considered compound-related) which matches the upper incidence of 6 percent in the glyphosate study. Toxicology Branch (TB) does not consider these random data as convincing.

However, based on a meeting held June 7, 1989 between W. Dykstra, E. Budd, and W. Burnam, TB concludes that a repeat of the mouse oncogenicity study is not required at this time. After the results of the new 2-year rat chronic toxicity and oncogenicity study are reviewed, TB will reconsider whether the repeat of the mouse oncogenicity study is required.

Background

On November 10, 1988, a meeting was held between EPA staff and representatives of Monsanto to discuss the Agency's requirement that the mouse oncogenicity study with glyphosate be repeated (memorandum attached).

Monsanto stated that there were historical control data demonstrating that the incidence of mouse kidney neoplasms ranged from 0 to 7.1 percent. This incidence exceeded the incidence of 6 percent from the high-dose group in the glyphosate study. Monsanto indicated that a repeat mouse oncogenicity study was not required.

EPA stated that the historical control data should be submitted in order to reevaluate the Agency's position on the repeat study.

In response to this request, Monsanto has submitted historical control data from several sources to substantiate their contention regarding the range of mouse kidney tumor neoplasms.

Review

1. The incidence of renal tubule tumors in the glyphosate mouse study is shown below:

	Mouse Kidney			
Dose (ppm)	0	1000	5000	30,000
No. Examined	49	49	50	50
Tubular Adenomas	1	0	1	3
Percent Incidence	2%	0%	2%	6%

2. The historical control data are presented below and are also attached to this memorandum.

   a. Bio/dynamics Historical Control Data - From studies initiated between 1976 and 1980 and terminated between 1978 and 1982, the incidence of tumors is shown below as submitted by Monsanto:

CD-1 COBS (ICR Derived) Mice
Bio/dynamics, Inc.
MALES - KIDNEYS

CONTROL DATA

STUDY I.D.	A	B	C	D	E	F	G	H*	I	J**	K+	L	M**	N	O	P
Tissue/Finding																
No. Examined	111	121	104	119	120	120	120	15	50		47	49		200	50	60
NEOPLASTIC FINDINGS																
B-Tubular Adenoma	1				2											
M-Tubular Carcinoma																

B = benign; M = malignant.
Control groups IA and IB counted together.
+ Study K = common control animals used for two test articles.
* = Gross Lesions only - kidney not routinely examined.
** = No microscopic findings recorded to date.

Note: Search for Renal Tubular Carcinomas revealed no incidence in these studies.

Male Charles River CD-1 Mice
Bio/dynamics, Inc.
KIDNEY

CONTROL DATA

STUDY I.D.	A		B		C		D		E		F		G	
	*	**	*	**	*	**	*	**	*	**	*	**	*	**
Tissue/Finding														
Neoplasm No. Examined	57	54	61	51	53	59	60	60	60	60	60	60	60	60
B - Tubular Adenoma		01								02				

*Control Group A	Start	6/78	12/77	12/77	10/78	11/78	11/77	10/77
**Control Group B	Terminate	7/80	4/80	3/80	4/81	4/81	4/80	4/80

Discussion

It can be seen from the above data that the range of historical controls of mouse renal neoplasms from Bio/dynamics is 0 to 3.3 percent. It should be noted that the glyphosate mouse oncogenicity study was conducted by Bio/dynamics between 1980 and 1982. Therefore, the 6 percent incidence of renal tumors in the high-dose group in the glyphosate mouse study exceeds the upper limit of the range of 3.3 percent in the historical

b. Hazleton's Historical Control Data

In a letter dated December 2, 1988 from J.M. Burns of Hazleton to D. Ward of Monsanto, six studies are cited as shown below:

The incidences are for scheduled sacrifices and unscheduled deaths combined.

Study	Type	Init.	Term.	Tubular Cell Carcinoma, Males
1	Dietary	3/80	3/82	2/43
2	Dietary	4/80	4/82	1/100
3	Dietary	9/81	9/83	0/80
4	Dietary	12/79	12/81	0/50
5	Dietary	5/82	5/84	0/50
6	Gavage	8/83	8/85	0/47

Tubular cell carcinomas only were observed.

Discussion

The range of mouse renal neoplasma cited by Hazleton is 0 to 4.7 percent. Therefore, the incidence of 6 percent in the high-dose group of the glyphosate mouse study exceeds the historical controls from Hazleton.

Additional, Monsanto has submitted "representative historical control data" from Hazleton reproduction studies in which renal neoplasia occurred in groups of F_1 generation control mice which were sacrificed after 91 to 105 weeks. These data are shown below:

NEOPLASIA IN CD-1® F_1 MICE - UNTREATED CONTROLS

FINDING	POSITIVE FINDINGS (MALES)	ANIMALS EXAMINED (MALES)
TISSUE NAME--KIDNEY		
TUBULAR CELL ADENOMA	1	15
	1	14
POSITIVE TOTALS	2	29
OVERALL TOTALS	2	56
OVERALL PERCENT	3.6	
RANGE OF PERCENTAGES	7	7
TUBULAR CELL CARCINOMA	1	15
POSITIVE TOTALS	1	15
OVERALL TOTALS	1	56
OVERALL PERCENT	1.8	
RANGE OF PERCENTAGES	7	7

Discussion

Apparently, this historical control data, which range from 0 to 7.1 percent, are the historical control data cited by Monsanto in their meeting with EPA on November 10, 1988. In a telephone communication on January 30, 1989 to Dr. Ward of Monsanto (314-694-8818), Dr. Ward indicated that Hazleton was unable to provide any additional details (dates of study, supplier, pathologists, etc.) about these particular historical controls. Therefore, in light of this telephone communication, TB concludes that these particular historical controls from F_1 male mice cannot be used to substantiate the Monsanto position.

C. IRDC Historical Control Data

Historical control data from IRDC on the incidences of renal neoplasms in CD-1 male mice in 19 studies of 24 to 25 month duration conducted between 1976 and 1978 are summarized below.

Tumors	No. Tumors	Range	No. Examined
Kidneys			1490
Adenoma	3	0-1.3	
Carcinoma	4	0-1.7	

Discussion

The range of 0 to 1.7 percent for renal neoplasms at IRDC does not exceed the incidence of 6 percent in the high-dose group of the glyphosate mouse study. The submitted historical control data from IRDC did not show the individual study incidences and therefore, is limited in this respect.

D. Spontaneous Renal Neoplasms Observed on 18 Food Color Additive Studies

Monsanto has submitted the incidence of renal neoplasms from 18 food color additive chronic studies with CD-1 mice (supplied to Monsanto by Dr. J.K. Haseman of NIEHS). These data are presented below:

INCIDENCE OF RENAL NEOPLASMS IN CONTROL MALE CD-1 MICE

Study ID[a/]	Testing Laboratory[b/]	Lesion Description	Incidence Group A	Incidence Group B
Blue No. 1	IRD	Cortical adenoma	0/60	1/60
Blue No. 2	B/d	Tubular cell adenoma	0/57	1/54
Green No. 3	B/d		0/51	0/53
Green No. 5	HL	Tubular cell adenoma	1/59	0/59
Yellow No. 5	IRD		0/60	0/60

a/A series of chronic bioassays in Charles River CD-1 mice were conducted on 18 food color additives. These studies were sponsored by the Certified Colors Manufacturers Association; the Cosmetic, Toiletries, and Fragrance Association; and the Pharmaceutical Manufacturers Association. Each study utilized 2 concurrent control groups of 60 mice/sex/group. These studies were conducted during the period of 1977 to 1980.

b/Testing laboratories were: International Research and Development Corporation (IRD); Bio/dynamics, Inc. (B/d); Hazleton Laboratories (HL); and Litton Bionetics (LB).

INCIDENCE OF RENTAL NEOPLASMS IN CONTROL MALE CD-1 MICE (Cont'd)

Study ID	Testing Laboratory	Lesion Description	Incidence Group A	Incidence Group B
Yellow No. 6	B/d		0/61	0/60
Yellow No. 10	B/d		0/60	0/60
Orange No. 5	B/d		0/60	0/60
Orange No. 17	B/d	Tubular cell adenoma	0/60	2/60
Red No. 3	IRD		0/60	0/60
Red No. 6	IRD		0/60	0/60
Red No. 9	LB	Tubular cell adenoma	0/59	2/60
Red No. 9		Tubular cell adenocarcinoma	1/59	0/60
		Cholesterol granuloma	1/59	0/60
Red No. 19	B/d		0/54	0/57
Red No. 21	IRD	Adenoma (N.O.S.)	1/60	0/60
Red No. 27	LB	Tubular cell adenoma	1/60	0/59
		Hemagiosarcoma	1/60	0/59
Red No. 30	HL		0/60	0/58
Red No. 33	IRD	Tubular cell adenoma	1/60	0/60
		Cortical carcinoma	1/60	0/60
Red No. 36	LB		0/60	0/60

Discussion

The incidence of renal tubular neoplasms ranged from 0 to 3.3 percent. It should be noted that the 3.3 percent incidence (2/60) of tubular cell adenoma in Orange No. 17 from Bio/dynamics was previously reported by Monsanto as historical

control data by Bio/dynamics and does not represent additional findings. The incidence of 3.3 percent (2/60) for renal tubular cell adenoma in Red No. 9 from Litton Bionetics was not previously reported and is considered new data.

E. Historical Control Data in CD-1 Mice From The Institute of Environmental Toxicology (Tokyo, Japan).

The incidence of renal neoplasms from male CD-1 mice was 6/891 (0.67%). In a telephone communication on January 30, 1989 with Dr. Ward of Monsanto, Dr. Ward indicated that for individual studies the incidence of renal neoplasms ranged from 0 to 1.4 percent (1/70). The range of 0 to 1.4 percent of renal neoplasms is comparable to the incidences observed at other laboratories.

Attachments

007252

R:53487:Dykstra:C.Disk:KENCO:2/6/89:CT:VO:CT
R:57213:Dykstra:C.Disk:KENCO:5/7/89:rw:vo:jh:dg

Attachment C
007252

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Glyphosate - Meeting with Monsanto Regarding EPA's Requirement that the Mouse Oncogenicity Study be Repeated

TOX Chem No.: 661A

FROM: Edwin Budd, Section Head
Toxicology Branch - Insecticide, Rodenticide Support
Health Effects Division (TS-769C)

11/15/88

TO: Robert J. Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (TS-767C)

On November 10, 1988, EPA staff met with representatives from Monsanto Company to discuss the Agency's requirement that the mouse oncogenicity study on glyphosate be repeated. The meeting was requested by Monsanto in a letter dated October 5, 1988 (attached), which also briefly outlined some of Monsanto's rationale supporting their contention that "there is no relevant scientific or regulatory justification for repeating the glyphosate mouse oncogenicity study." The following persons attended the meeting:

EPA Staff	Monsanto Company
Anne Lindsay	Chester Dickerson, Jr.
Frank Sanders	Kevin Cannon
Robert J. Taylor	Dennis Ward
William Burnam	
Edwin Budd	

Dennis Ward initiated the meeting by recounting pertinent findings in the rat and mouse oncogenicity studies on glyphosate, recalling prior EPA and SAP assessments of the available data,

presenting Monsanto's rationale and conclusions regarding the totality of the available data relating to the oncogenic potential of glyphosate, and reiterating Monsanto's contention that there is no scientific or regulatory justification for repeating the mouse study. Highlights of his presentation are itemized in a document handed out at the meeting (attached).

In response to Dennis Ward's presentation, Edwin Budd said he did not recall having previously seen historical control data on kidney tumors in mice with a range in individual studies of 0 to 7.1 percent. Dr. Ward stated that he believed this information (on individual studies) had been submitted to EPA some time ago. Inasmuch as a major reason for EPA's concern regarding the kidney tumors in the mouse study was the belief that such tumors are quite rare in mice, the meeting participants agreed that it would be appropriate to again consider relevant historical control data on the matter, and particularly the findings in individual studies. Toward this end, Monsanto agreed to locate and again submit to the Agency as soon as possible what they believe to be pertinent historical control data on individual studies. EPA, in turn, agreed to evaluate the usefulness and content of the data and utilize it, as appropriate, in a reconsideration of EPA's prior requirement that the mouse study be repeated.

Attachments

cc: William Burnam
Judith Hauswirth
William Dykstra

Monsanto

Monsanto Company
1101 17th Street, N.W.
Washington, D.C. 20036
Phone (202) 452-8860

October 5, 1988

Director
Registration Division (TS767C)
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Crystal Mall #2, Room 1116
Arlington, Virginia 22202

Attention: Mr. Edwin F. Tinsworth

Subject: Glyphosate Registration Standard: Request for Meeting with EPA

Dear Sir:

On September 7, 1988 the Agency submitted to Monsanto a scientific review and evaluation of our November 7, 1986 response to the glyphosate Registration Standard issued in August, 1986. Part of that response included a request for a waiver of the requirement to repeat the glyphosate mouse oncogenicity study. The Agency's letter indicates that you have decided not to concur with our waiver request and have asked for Monsanto "to conduct a specially designed study for the specific purpose of clarifying certain unresolved questions relating to the potential oncogenicity of glyphosate."

Monsanto's position regarding this requirement has been, and remains to be, that there is no scientific justification for repeating the mouse oncogenicity study. The results of the current mouse oncogenicity study have been reviewed by numerous toxicologists and pathologists from both the private sector and universities, as well as by the FIFRA Scientific Advisory Panel. The unanimous conclusion of all of these experts was that this study did not provide evidence that glyphosate was oncogenic to mice. The study was conducted at dosages far in excess of those required by the Agency's MTD Position Paper, and the response in question (a spurious, not statistically significant increase in a benign kidney tumor) occurred in only three male mice at a dosage level of 30,000 ppm glyphosate in the diet.

Repeating this study will not provide any new information which would be useful for regulatory purposes. Monsanto has analyzed the effects of dosage levels, tumor dose response and number of animals tested on the hypothetical Q1* which would result. In the twenty cases we analyzed, which covered dosage levels and group sizes including those suggested by the Agency for a repeat study, it was clear that there was no significant difference in the calculated Q1* values. This was true even when the hypothetical tumor response rate was double that observed in the original mouse study. Multiplying the very low calculated Q1*'s by the low level of potential human exposure to glyphosate (1) results in potential levels of human risk far less than 1 x 10 -6.

The low values obtained for the calculated Q1*'s and their insensitivity to percent tumor response and number of animals tested underscore the lack of value in conducting another study to characterize glyphosate in EPA's ranking scheme. Monsanto believes it may be more useful to use the results of the ongoing repeat rat chronic feeding/oncogenicity study to determine whether any change from the current "D" classification is in order.

Based upon the above discussion, Monsanto contends that there is no relevant scientific or regulatory justification for repeating the glyphosate mouse oncogenicity study. We feel that to do so would not be an appropriate use of either the Agency's or Monsanto's resources. I would like to have the opportunity to meet with you to review this issue in further detail, and have asked Dr. Kevin Cannon to contact Mr. Robert Taylor to schedule a mutually agreeable date. I would like to suggest October 19, 1988 as a possibility.

Thank you for your attention to this issue, and if you should have any questions regarding this request, please contact either Dr. Kevin Cannon in our Washington office or me.

Sincerely,

George B. Fuller, Ph.D.
United States and International
Registration Director

References

1. An excellent review of potential human risks from exposure to glyphosate under hypothetical "worst case" scenarios can be found in a document prepared by K.S. Crump and Associates for the state of Washington, Department of Natural Resources: Shipp, A.M. et al. (1986). Worst Case Analysis Study On Forest Plantation Herbicide Use. See specifically Chapter 5. Risk Assessment for Glyphosate, pp. 132-140.

/bj
cc: K.F. Cannon

handed out by Monsanto at whole meeting

Meeting with EPA, November 10, 1988 on:

007252

GLYPHOSATE -- ISSUES RELATED TO ONCOGENICITY

1. Rat study -- No treatment related tumors; however, an MTD was not achieved. Replacement study in progress.

2. Mouse study -- Ongoing disagreement over interpretation of kidney tumors in male mice:

Dose Level (ppm)	0	1000	5000	30,000
Tubular adenoma	1	0	1	3
Animals examined	49	49	50	50

3. Monsanto conclusion -- These tumors are not treatment related:

- lack of significance in pair-wise comparison test;
- lack of significance in age-adjusted trend test;
- high dose incidence is within historical control ranges (0-7.1%);
- mechanistic considerations: glyphosate is not metabolized by rodents and is not genotoxic; promotional mechanism is unlikely due to lack of cytotoxicity, inflammatory responses, or preneoplastic changes in target organ;
- unanimous conclusion of third party pathologists that these tumors are not treatment related;
- FAO/WHO has concluded "... no evidence of carcinogenicity".

4. S.A.P. conclusion - Equivocal, Category D

   - small number of tumors at HDT which appears to have exceeded the MTD
   - "... no oncogenic effect of Glyphosate is demonstrated using concurrent controls."
   - "... the level of concern raised by historical control data was not great enough to displace putting primary emphasis on the concurrent controls."

5. Toxicology Branch conclusion - "... the oncogenic potential of glyphosate could not be determined from existing data and proposes that the study be repeated in order to clarify these equivocal findings."

6. Monsanto continues to believe that a weight-of-evidence evaluation strongly supports conclusion that glyphosate is not oncogenic in the mouse. Results of the ongoing chronic rat study will answer questions about oncogenic potential of glyphosate.

7. Repeating the mouse study is unlikely to "... clarify these equivocal findings." Answering this academic question would require the expenditure of significant resources, the wasting of hundreds of additional laboratory animals, and would tie-up valuable laboratory space.

8. Repeating the mouse study would have no impact on the regulatory management of glyphosate, regardless of study outcome. Estimates of risk could only decrease (refer to attached tables).

Table 1. Effect of group size (n) on linearized multistage model slope (q_1^*) with a constant tumor response rate.

	Tumor Incidence (%)				
Group Size	0	1000	5000	30,000	q_1^* $(mg/kg/d)^{-1}$
n = 50	2	0	2	6	3.2×10^{-4}
n = 100	2	0	2	6	2.6×10^{-4}
n = 200	2	0	2	6	2.2×10^{-4}

Dose levels of 0, 1000, 5000 and 30,000 ppm in diet correspond to human equivalent doses $(BW)^{0.67}$ of 0, 12.5, 64.6, and 384 mg/kg/d.

Table 2. Effect of group size (n) and hypothetical tumor response rate on linearized multistage model slope (q_1^*).

Group Size	Tumor Incidence (%) 0	7500	15,000	30,000 ppm	q_1^* $(mg/kg/d)^{-1}$
n = 50	2	0	2	6	1.9×10^{-4}
n = 200	2	0	2	6	7.0×10^{-5}
n = 200	0	0	0	12	2.9×10^{-5}
n = 200	0	0	4	12	1.5×10^{-4}

Dose levels of 0, 7500, 15,000 and 30,000 ppm in diet correspond to human equivalent doses $(BW)^{0.67}$ of 0, 96.0, 192, and 384 mg/kg/d.

Monsanto

Monsanto Company
1101 - 17th Street N.W.
Washington D.C. 20036
(202) 452-8880

Chester T. Dickerson, Jr., Ph.D.
Director, Agricultural Affairs

Monsanto

Monsanto Company
1101 17th Street N.W.
Suite 604
Washington, D.C. 20036
(202) 452-8880

Kevin F. Cannon, Ph.D.
Manager, Agricultural Affairs

Monsanto

Monsanto Agricultural Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
(314) 694-8818

Dennis P. Ward, Ph.D.
Diplomate, American Board of Toxicology
Product Toxicology Specialist

GLYPHOSATE

Page_____ is not included in this copy.

Pages 19 through 23 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

X CLAIMED CONFIDENTIAL BY REGISTRANT

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

APPENDIX A:

Bio/dynamics Historical Control Data

GLYPHOSATE

Page_____ is not included in this copy.

Pages 25 through 31 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

APPENDIX B:

Hazleton Historical Control Data

GLYPHOSATE

Page_____ is not included in this copy.

Pages 33 through 40 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

APPENDIX C:

IRDC Historical Control Data

GLYPHOSATE

Page_____ is not included in this copy.

Pages 42 through 50 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

APPENDIX D:

Spontaneous Renal Neoplasms Observed on

18 Food Color Additive Studies

GLYPHOSATE

Page 52 is not included in this copy.

Pages _____ through _____ are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

APPENDIX E:

Historical Control Data in CD-1 Mice from

The Institute of Environmental Toxicology

GLYPHOSATE

Page_____ is not included in this copy.

Pages 54 through 63 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.